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Toxic Overdose of Antiepileptic Lacosamide: A Rare Case Report

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Abstract

Lacosamide (LCM), a third generation antiepileptic drug, is used as an adjunctive therapy or monotherapy in focal seizures. It enhances slow inactivation of voltage gated sodium channels and acts on collapsin-response mediator protein-2. Toxic ingestion of lacosamide has been documented and patients developed severe neurological and cardiac manifestation and few cases were fatal. Currently, there isno antidote for lacosamide poisoning. The poisoned patients are managed conservatively. Inj. sodium bicarbonate therapy was given in few cases to correct for cardiac arrhythmia. In many reported cases multiple tablets were consumed for poisoning except one case report documentedisolated ingestion of lacosamide. We report a case of acute overdose of isolated lacosamide poisoning who was brought to our emergency department in an unresponsive state with a history of seizure.

Keywords: Antiepileptics poisoning; Lacosamide poisoning; Sodium bicarbonate therapy; Torsades de pointes.

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Introduction

Lacosamide(LCM), a third generation antiepileptic drug, is used as a adjunctive therapy or monotherapy in focal seizures.[1] It acts by selectively enhancing slow inactivation of voltage gated sodium channels and also act on collapsin-response mediator protein 2 (CRMP-2) and thereby increasing seizure threshold.[2] The pharmacokinetics of LCM include 100% bioavailability on ingestion, volume of distribution of 0.6L/kg, half life of 13 hours(h) and attains peak concentration in 0.5-4h.[3] On therapeutic dosage It's adverse effect are similar to other sodium channel blocking agents which includes dizziness (30%), headache, diplopia, nausea and vomiting. It causes mild PR prolongation with therapeutic drug level.[1] Patients taking lacosamide in excess developed cardiac and neurological manifestations as similar to sodium channel blocker poisoning and death was documented in few reports.[4-9] There is no antidote for lacosamide poisoning and in few cases Inj. Sodium bicarbonate was given to correct cardiac arrhythmia. We report a case of isolated lacosamide poisoning who was brought unconscious to our emergency department (ED) with a history of seizure and had ventricular tachycardia. Patient was intubated for poor GCS score and symptomatically managed, shewas extubated when her consciousness improved and got discharged in a week.

Case Report

A 34 year old female who was on tablet lacosamide 100mg bid for seizure disorder brought to the ED with alleged history of taking 30 tablets of

lacosamide 100 mg after a quarrel with her husband. She had one episode of Generalised tonic clonic seizure (GTCS) after half an hour of poisoning and was unresponsive since then.

Her initial vital signs were: BP -130/80 mm of Hg, Pulse rate-126/min, Respiratory rate-20, SpO2- 97% in room air, blood glucose- 106mg/dl. On examination her GCS was-E1V1M2, pupils bilateral 3 mm and equally reactive to light, her lung and cardiac auscultation were normal. She had an episode of GTCS which was controlled with injection of lorazepam 2mg. Further she had 2 more episodes of GTCS which was brief. Patient was intubated with injection propofol. ECG monitor showed non- sustained ventricular tachycardia and frequent premature ventricular complex and she was given a bolus of Inj. Sodium bicarbonate 50 mEq. No further episode of VT and seizure witnessed. Initial ECG was taken immediately after bolus dose of Inj. Sodium bicarbonate which showed sinus tachycardia, heart rate-125, prolonged P wave(P-113ms), QRS-153ms, QT interval -467ms, complete right bundle branch block with ST depressions in V4-V6, positive terminal R wave in aVR. (fig. 1)

In repeat ecg tachycardia persists but QRS duration shortened to 146ms and QT interval-423ms. (fig. 2)

Patient was put on ventilatory support and Inj Sodium bicarbonate 100mEq in 500ml 5% dextrose was given along with other supportive care. Patient attained consciousness on the next day and improved without any neurological deficit. She was extubated on the 2nd day and her ECG showed heart rate-98, QRS -105ms, QTc- 426ms and RBBB morphology. (fig. 3)

Her renal and liver function parameters were normal. Serum level of lacosamide was not done to determine the peak concentration in patient blood due to its non-availability. Patient recovered and she was discharged on the 5th day.

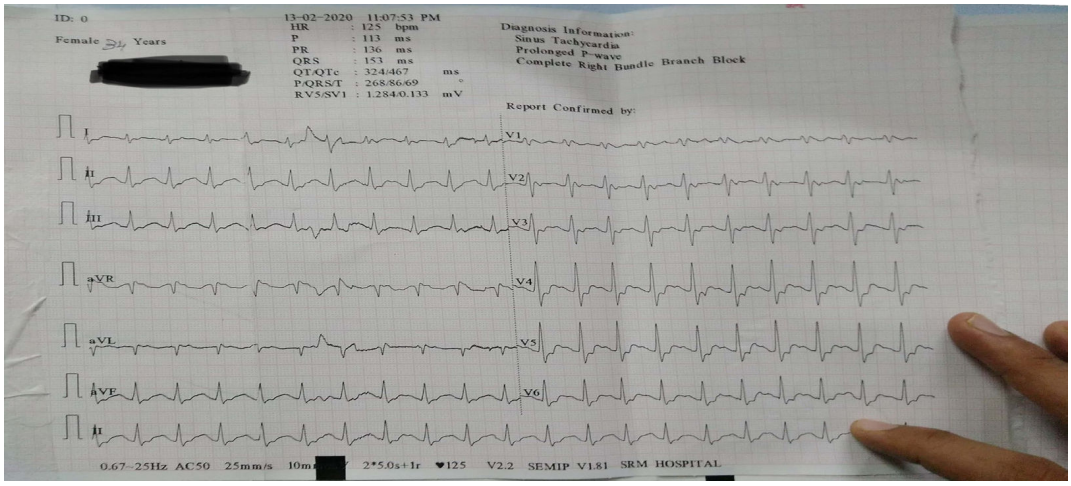

Fig. 1: ECG- Awide complex regular sinus tachycardia, rate-125, QRS duration-153 ms, QTc- 467ms, RBBB Morphology.

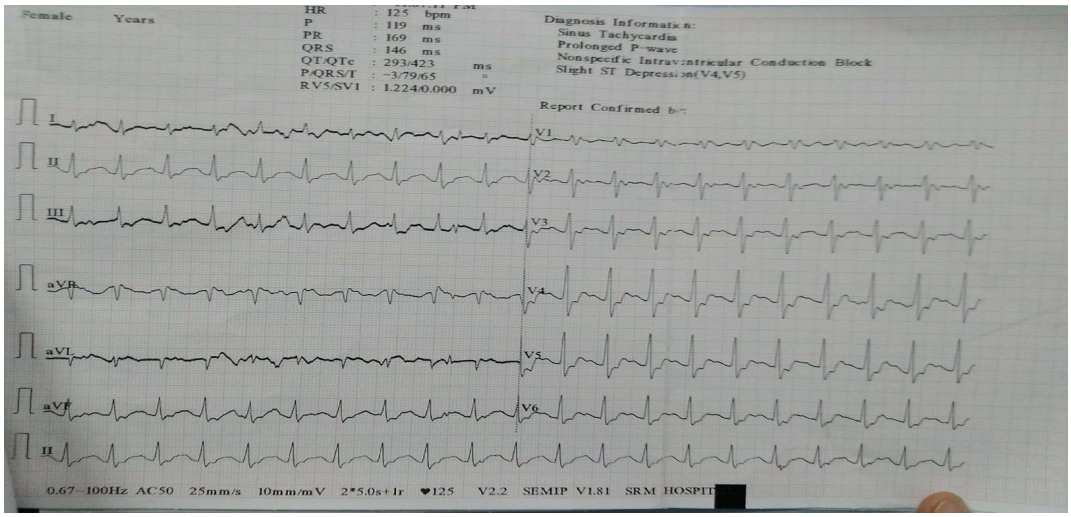

Fig. 2: ECG- A wide complex regular sinus tachycardia, rate- 125, QRS duration-423 ms, QTc-423 ms, RBBB Morphology.

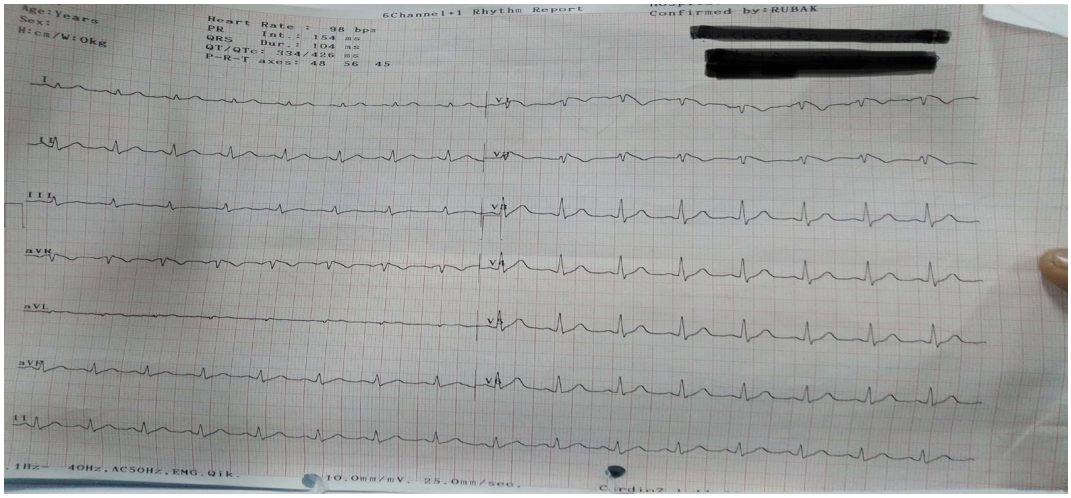

Fig. 3: ECG- Sinus rhythm with heart rate-98, QRS duration-104ms, QTc-423ms, RBBB Morphology.

Discussions

Lacosamide is an anti epileptic drug, approved by the FDA for partial seizure particularly in refractory seizures.[1] Since it attains peak concentration in 0.5-4 h and its oral bioavailability is 100%, patients may show toxic features very early. Most of the reported patients developed symptoms within an hour of taking the tablets.(4-9) Our patient had seizure within 0.5 h after ingestion of tablet ingestion.

In future, the use of lacosamide as monotherapy for focal seizures and status epilepticus may increase considering the pharmacokinetics of the drug and its mechanism of action particularly disease modifying effect by regulating the neuronal outgrowth(CRMP-2).[1,2,7]

Our patient took tablet lacosamide alone for poisoning and the patient accepted it once she became conscious and extubated. To our knowledge, this is the second report of a large-quantity isolated lacosamide overdose.[7] Till now only three cases of cardiac arrests associated with ingestion of lacosamide have been reported in the literature. In all three cases lacosamide was coingested along with at least one another drug.[5,8]

A poison centre study found that the occurrence of seizure in patients with lacosamide ingestion is 17%.(10) Most of the reported lacosamide poisoning cases had seizure as their presenting symptom.[4,6,7,9,11] Cardiac manifestation is rare in therapeutic dosage and ECG may show mild PR prolongation in some cases. One patient with lacosamide poisoning had pulseless VT on initial presentation which reverted with cardiac defibrillation.[5] In this case we noticed non-sustained VT which got controlled when Inj. Sodium bicarbonate was given for correcting QRS prolongation. Considering the termination of VT after sodium bicarbonate bolus, we can assume the therapeutic role of sodium bicarbonate in lacosamide poisoning. Sodium bicarbonate was given in four cases for QRS prolongation; one had no significant change, another showed further widening which was suspected due to ongoing absorption of drug whereas in other two cases narrowing of QRS was documented.[5-8] In this case there was mild shortening of QRS duration was present immediately (153ms to 146 ms) and ECG on second day showed significant QRS duration shortening (106ms). Despite inadequate evidence supporting the role of sodium bicarbonate as an antidote for LCM poisoning,Our patient was completely recovered with sodium bicarbonate infusion and supportive care. Hemodialysis was not done in our patient whereas a comatose patient showed complete neurological recovery after hemodialysis.[9]

Therapeutic drug monitoring was not done due to its non-availability in our setup. Inj sodium bicarbonate and hemodialysis can be considered while managing a patient with LCM overdose. Complete recovery can be expected when managed appropriately.

Conclusion

Large dose ingestion of lacosamide can be fatal either due to arrhythmia(Ventricular tachycardia and torsades de pointes) or status epilepticus. Since there is no antidote, patients are managed conservatively. injection Sodium bicarbonate are given as supportive therapy in patients having no contraindication. Early identification of changes in ECG and cardiac monitoring may help to avoid potentially fatal complications.

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12. Figure 1. ECG- Awide complex regular sinus tachycardia, rate-125, QRS duration-153 ms, QTc- 467ms, RBBB Morphology.
13. Figure 2. ECG- A wide complex regular sinus tachycardia, rate- 125, QRS duration-423 ms, QTc-423 ms, RBBB morphology.
14. Figure 3. ECG- Sinus rhythm with heart rate-98, QRS duration-104ms, QTc-423ms, RBBB morphology.